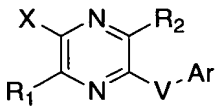
CLAIMS

1. A compound of Formula I or a stereoisomer, pharmaceutically acceptable salt, or a prodrug thereof



Formula I

X is selected from $-NR_3R_4$, $-OR_3$, $-CR_3R_5R_5$, $-C(O)R_3$, $-S(O)_mR_3$, $-NR_3C(O)R_4$, $-NR_3S(O)_mR_4$;

V is selected from -O-, $-NR_5$, or $-S(O)_m$;

m is 0,1 or 2;

R_1 and R_2 are independently selected from -NH(alkyl), $-N(alkyl)_2$, -NH(substituted alkyl), $-N(substituted\ alkyl)_2$, -O(alkyl), -O(substituted alkyl), halogen, alkyl, substituted alkyl, haloalkyl, cycloalkyl, substituted cycloalkyl, substituted phenyl, naphthyl, substituted naphthyl, heteroaryl, heteroaryl derivatives, substituted aryl, heterocycloalkyl, substituted heterocycloalkyl, substituted heteroaryl, $-CR_5R_6Ar$, -OAr, $-S(O)_mAr$, $-NR_5Ar$, $-S(O)_m$alkyl, $-S(O)_m$substituted alkyl, $-NO_2$, -OH, $-NH_2$, -SH, $-C(O)NR_4R_5$,$-C(S)NR_4R_5$, $-C(O)NR_5Ar$, $-S(O)_mNR5Ar$, $-NR_5C(O)Ar$, $-NR_5S(O)nAr$, -C(O)Ar, -(alkyl linker)$S(O)_mNH_2$, -(alkyl linker)$S(O)_mNR_5Ar$, and -(alkyl linker)C(O)Ar;

R_3 and R_4 are independently selected from -H, alkyl, substituted alkyl, haloalkyl, cycloalkyl, substituted cycloalkyl, aryl, heterocycloalkyl, substituted heterocycloalkyl, substituted heteroaryl, aryl cycloalkyl, substituted aryl cycloalkyl, heteroaryl cycloalkyl, substituted heteroaryl cycloalkyl, aryl heterocycloalkyl, substituted aryl heterocycloalkyl, heteroaryl heterocycloalkyl, or substituted heteroaryl heterocycloalkyl;

Each R_5 is independently selected from -H, alkyl, alkylene, alkylyne, cycloalkyl, haloalkyl, and alkyl substituted with 1-3 substituents selected from halogen, -O(alkyl), -NH(alkyl), $-N(alkyl)_2$, -C(O)NH(alkyl), $-C(O)N(alkyl)_2$, -NHC(O)alkyl, -N(alkyl)C(O)alkyl, $-S(O)_m$alkyl, heterocycloalkyl, substituted heterocycloalkyl and Ar.

Each R_6 is independently selected from alkyl, cycloalkyl, haloalkyl, and alkyl substituted with 1-3 substituents selected from halogen, -O(alkyl), -NH(alkyl), -

$N(alkyl)_2$, -C(O)NH(alkyl), $-C(O)N(alkyl)_2$, -NHC(O)alkyl, -N(alkyl)C(O)alkyl, $-S(O)_m$alkyl, heterocycloalkyl, substituted heterocycloalkyl and Ar;

Halogen is a group selected from -F, -Cl, -Br, -I;

Alkyl means both straight- and branched chain hydrocarbon chains having from 1-10 carbon atoms;

Alkylene means both straight- and branched chain hydrocarbon chains having from 2-10 carbon atoms and a double bond;

Alkylyne means both straight- and branched chain hydrocarbon chains having from 2-10 carbon atoms and a triple bond;

Substituted alkyl is an alkyl moiety from 1-10 carbon atoms having 1-3 substituents independently selected from halogen, $-S(O)_mR_5$, $-NR_5R_5$, $-C(O)R_5$, -CN, $-C(O)NR_5R_5$, $-NR_5C(O)R_5$, $-S(O)_mNR_5R_5$, $-NR_5S(O)_mR_5$, CN, $-NO_2$, and Ar;

Haloalkyl is an alkyl moiety having from 1-10 carbon atoms and having 1 to (2v+1) independently selected halogen substituent(s) where v is the number of carbon atoms in the moiety;

Cycloalkyl is a monocyclic or bicyclic alkyl moiety, having from 3-10 carbon atoms optionally containing 1 to 2 double bonds provided that the moiety is not aromatic, and further provided that the double bonds are not cumulated;

The term "substituted cycloalkyl" is a cycloalkyl group having 1-3 substituents independently selected from halogen, $-R_5$, $-OR_5$, $-S(O)_mR_5$, $-NR_5R_5$, $-C(O)R_5$, -CN, $-C(O)NR_5R_5$, $-NR_5C(O)R_5$, $-S(O)_mNR_5R_5$, $-NR_5S(O)_mR_5$, and $-NO_2$;

Alkyl linker means a group selected from alkyl, substituted alkyl, haloalkyl, cycloalkyl, and substituted cycloalkyl having two points of attachment;

The term "heterocycloalkyl", unless otherwise specified, means a 4 to 8 membered monocylic ring or bicyclic ring, wherein at least one carbon atom is replaced with a heteromember selected from oxygen, nitrogen, -NH-, or $-S(O)_m-$ wherein m is zero, 1, or 2, optionally containing from one to three double bonds, provided that the molecule is not aromatic; and provided that ring attachment can occur at either a carbon or nitrogen atom;

The term "substituted heterocycloalkyl" is a heterocycloalkyl group having 1-3 substituents independently selected from halogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, $-OR_5$, $-S(O)_mR_5$, $-NR_5R_5$, $-C(O)R_5$, -CN, $-C(O)NR_5R_5$, $-NR_5C(O)R_5$, $-S(O)_mNR_5R_5$, $-NR_5S(O)_mR_5$, and $-NO_2$;

Substituted phenyl is a phenyl group having 1-3 substituents independently selected from halogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, -OR_5, SR_5, -NR_5R_5, -$C(O)R_5$, -CN, -$C(O)NR_5R_5$, -$NR_5C(O)R_5$, -$S(O)_mNR_5R_5$, -$NR_5S(O)_mR_5$, and -NO_2;

Substituted napthyl is a napthyl group having 1-3 substituents independently selected from halogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, -OR_5, SR_5, -NR_5R_5, -$C(O)R_5$, -CN, -$C(O)NR_5R_5$, -$NR_5C(O)R_5$, -$S(O)_mNR_5R_5$, -$NR_5S(O)_mR_5$, and -NO_2;

The term "heteroaryl" means a radical attached via a ring carbon or nitrogen atom of a monocyclic aromatic ring containing five or six ring atoms consisting of carbon and 1, 2, 3, or 4 heteroatoms each selected from the group consisting of non-peroxide O, S, N, with appropriate bonding to satisfy valence requirements as well as a radical (attachment at either carbon or nitrogen) of a fused bicyclic heteroaromatic of about eight to ten ring atoms;

The term "substituted heteroaryl" means a heteroaryl group having 1-3 substituents independently selected from halogen, -R_5, -OR_5, -$S(O)_mR_5$, -NR_5R_5, -$C(O)R_5$, -CN, -$C(O)NR_5R_5$, -$NR_5C(O)R_5$, -$S(O)_mNR_5R_5$, -$NR_5S(O)_mR_5$, and -NO_2, phenyl, substituted phenyl, napthyl, substituted napthyl, heteroaryl, and heteroaryl derivatives;

The term "heteroaryl derivatives" means a heteroaryl group having 1-3 substituents independently selected from halogen, -R_5, -OR_5, -$S(O)_mR_5$, -NR_5R_5, -$C(O)R_5$, -CN, -$C(O)NR_5R_5$, -$NR_5C(O)R_5$, -$S(O)_2NR_5R_5$, -$NR_5S(O)_2R_5$, and -NO_2;

Aryl is selected from phenyl, napthyl, substituted phenyl, substituted napthyl, heteroaryl, and substituted heteroaryl derivatives;

Ar is selected from aryl, substituted aryl, and substituted heteroaryl;

The term "aryl cycloalkyl" means a bicyclic ring system containing 9 to 14 carbon atoms wherein one ring is aryl and the other ring is fused to the aryl ring and may be fully or partially saturated in the portion of the ring not fused to the aryl ring, provided that either ring may act as a point of attachment;

The term "substituted aryl cycloalkyl" means an aryl cycloalkyl group having 1-3 substituents independently selected from halogen, -R_5, -OR_6, -$S(O)_mR_5$, -NR_5R_5, -$C(O)R_5$, -CN, -$C(O)NR_5R_5$, -$NR_5C(O)R_5$, -$S(O)_mNR_5R_5$, -$NR_5S(O)_mR_5$, and -NO_2;

The term "heteroaryl cycloalkyl" means a bicyclic ring system containing 9 to 14 atoms, wherein one ring is heteroaryl and the other ring is fused to the aryl ring and may be fully or partially saturated in the portion of the ring not fused to the aryl ring, provided that either ring may act as a point of attachment;

The term "substituted heteroaryl cycloalkyl" means a heteroaryl cycloalkyl having 1-3 substituents independently selected from halogen, $-R_5$, $-OR_5$, $-S(O)_mR_5$, $-NR_5R_5$, $-C(O)R_5$, -CN, $-C(O)NR_5R_5$, $-NR_5C(O)R_5$, $-S(O)_mNR_5R_5$, $-NR_5S(O)_mR_5$, and $-NO_2$;

The term "aryl heterocycloalkyl" means a bicyclic ring system containing 9 to 14 atoms, wherein one ring is aryl and the other ring is heterocycloalkyl, provided that either ring may act as a point of attachment;

The term "substituted aryl heterocycloalkyl" means an aryl heterocycloalkyl having 1-3 substituents independently selected from halogen, $-R_5$, $-OR_5$, $-S(O)_mR_5$, $-NR_5R_5$, $-C(O)R_5$, -CN, $-C(O)NR_5R_5$, $-NR_5C(O)R_5$, $-S(O)_mNR_5R_5$, $-NR_5S(O)_mR_5$, and $-NO_2$.

The term "heteroaryl heterocycloalkyl" means a bicyclic ring system containing 9 to 14 atoms, wherein one ring is heteroaryl and the other ring is heterocycloalkyl, provided that either ring may act as a point of attachment;

The term "substituted heteroaryl heterocycloalkyl" means an heteroaryl heterocycloalkyl having 1-3 substituents independently selected from halogen, $-R_5$, $-OR_5$, $-S(O)_mR_5$, $-NR_5R_5$, $-C(O)R_5$, -CN, $-C(O)NR_5R_5$, $-NR_5C(O)R_5$, $-S(O)_mNR_5R_5$, $-NR_5S(O)_mR_5$, and $-NO_2$.

2. A pharmaceutical composition comprising a compound according to Claim 1 and at least one pharmaceutically acceptable carrier or excipient.

3. A method for the treatment or prevention of physiological disorders associated with excess of or insufficient amount of CRF, the method comprising administration to a patient in need thereof an effective amount of a compound according to Claim 1.

4. A method of inhibiting the binding of CRF to the CRF_1 receptor, the method comprising contacting, in the presence of CRF, a solution comprising a compound of Claim 1 with cells expressing the CRF_1 receptor, wherein the compound is present in the solution at a concentration sufficient to reduce levels of CRF binding to IMR32 cells in vitro.

5. A compound according to Claim 1 wherein the compound exhibits an IC50 for CRF binding of 1 micromolar or less.

6. A compound according to Claim 5 wherein the compound exhibits an IC50 for CRF binding of 100 nanomolar or less.

7. A compound according to Claim 6 wherein the compound exhibits an IC50 for CRF binding of 10 nanomolar or less in a standard assay of CRF binding.

8. A method for treating stress, anxiety or depression comprising administering to a patient in need thereof an effective amount of a compound according to Claim 1.

9. A compound according to claim 1 wherein V is O.

10. A compound according to claim 1 wherein V is NR_5.

11. A compound according to claim 1 wherein V is S.

12. A compound according to claim 1 wherein Ar is aryl.

13. A compound according to claim 1 wherein Ar is substituted aryl.

14. A compound according to claim 1 wherein Ar is substituted heteroaryl.

15. A compound according to claim 1 selected from the group consisting of

(1R,2S)-1-({3,6-diethyl-5-[(4-methylpyridin-2-yl)oxy]pyrazin-2-yl}amino)-2,3-dihydro-1H-inden-2-ol,

N-[(1R,2S)-2-ethoxy-2,3-dihydro-1H-inden-1-yl]-3,6-diethyl-5-[(4-methylpyridin-2-yl)oxy]pyrazin-2-amine,

3,6-diethyl-N-[(1R,2S)-2-(2-fluoroethoxy)-2,3-dihydro-1H-inden-1-yl]-5-[(4-methylpyridin-2-yl)oxy]pyrazin-2-amine,

3,6-diethyl-N-[(1R,2S)-2-isopropoxy-2,3-dihydro-1H-inden-1-yl]-5-[(4-methylpyridin-2-yl)oxy]pyrazin-2-amine,

3,6-diethyl-5-[(4-methylpyridin-2-yl)oxy]-N-[(1R,2S)-2-propoxy-2,3-dihydro-1H-inden-1-yl]pyrazin-2-amine,

(1R,2S)-1-({3,6-diethyl-5-[(4-methylpyridin-2-yl)oxy]pyrazin-2-yl}amino)-2,3-dihydro-1H-inden-2-yl acetate,

(1R,2S)-1-({3,6-diethyl-5-[(4-ethylpyridin-2-yl)oxy]pyrazin-2-yl}amino)indan-2-ol,

N-[(1R,2S)-2-ethoxy-2,3-dihydro-1H-inden-1-yl]-3,6-diethyl-5-[(4-ethylpyridin-2-yl)oxy]pyrazin-2-amine,

(1R,2S)-1-({3,6-diethyl-5-[(3-methylpyridin-2-yl)oxy]pyrazin-2-yl}amino)indan-2-ol,

N-[(1R,2S)-2-ethoxy-2,3-dihydro-1H-inden-1-yl]-3,6-diethyl-5-[(3-methylpyridin-2-yl)oxy]pyrazin-2-amine,

(1R,2S)-1-({3,6-diethyl-5-[(5-methylpyridin-2-yl)oxy]pyrazin-2-yl}amino)indan-2-ol,

N-[(1R,2S)-2-ethoxy-2,3-dihydro-1H-inden-1-yl]-3,6-diethyl-5-[(5-methylpyridin-2-yl)oxy]pyrazin-2-amine,

5-[(4,6-dimethylpyridin-2-yl)oxy]-N-[(1R,2S)-2-ethoxy-2,3-dihydro-1H-inden-1-yl]-3,6-diethylpyrazin-2-amine,

N-[(1R,2S)-2-ethoxy-2,3-dihydro-1H-inden-1-yl]-3,6-diethyl-5-(3-methylphenoxy)-pyrazin-2-amine,

1-({3,6-diethyl-5-[(4-methylphenyl)amino]pyrazin-2-yl}amino)indan-2-ol,

N-(2-ethoxy-2,3-dihydro-1H-inden-1-yl)-3,6-diethyl-5-[(4-methylphenyl)thio]pyrazin-2-amine,

3,6-diethyl-N-[(1R,2S)-2-(2-fluoroethoxy)-2,3-dihydro-1H-inden-1-yl]-5-[(4-methylpyridin-2-yl)oxy]pyrazin-2-amine, and

N-[(1R,2S)-2-ethoxy-2,3-dihydro-1H-inden-1-yl]-3,6-diethyl-5-[(4-methylpyridin-2-yl)oxy]pyrazin-2-amine.